FORM-I CRYSTAL OF 2-{4-[N-(5,6-DIPHENYLPYRAZIN-2-YL)-N-ISOPROPYLAMINO]BUTYLOXY}-N-(METHYLSULFONYL)ACETAMIDE AND METHOD FOR PRODUCING THE SAME

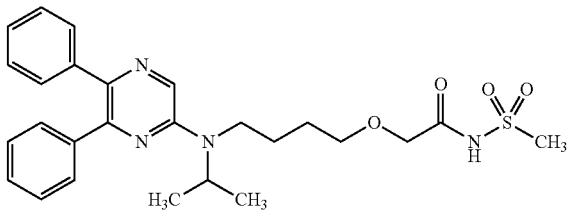
CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a U.S. national stage application under 35 U.S.C. §371 of International Patent Application No. PCT/JP2010/060798 filed on Jun. 25, 2010, which claims the benefit of foreign priority to Japanese Patent Application No. UP 2009-151727 filed on Jun. 26, 2009, Japanese Patent Application No. JP 2009-151728 filed on Jun. 26, 2009, and Japanese Patent Application No. JP 2009-151729 filed on Jun. 26, 2009, the disclosures of all of which are hereby incorporated by reference in their entireties. The International Application was published in Japanese on Dec. 29, 2010, as International Publication No. WO 2010/150865 A1 under PCT Article 21(2).

FIELD OF THE INVENTION

The present invention relates to a crystal of 2-{4-[N-(5,6-diphenylpyrazin-2-yl)-N-isopropylamino]butyloxy}-N-(methylsulfonyl)acetamide (hereinafter referred to as "compound A").

[Formula 1]



BACKGROUND OF THE INVENTION

Compound A has an excellent PGI2 agonistic effect and shows a platelet aggregation inhibitory effect, a vasodilative effect, a bronchodilative effect, a lipid deposition inhibitory effect, a leukocyte activation inhibitory effect, etc. (see, for example, in WO 2002/088084 ("WO '084")).

Specifically, compound A is useful as preventive or therapeutic agents for transient ischemic attack (TIA), diabetic neuropathy, diabetic gangrene, peripheral circulatory disturbance (e.g., chronic arterial occlusion, intermittent claudication, peripheral embolism, vibration syndrome, Raynaud's disease), connective tissue disease (e.g., systemic lupus erythematosus, scleroderma, mixed connective tissue disease, vasculitic syndrome), reocclusion/restenosis after percutaneous transluminal coronary angioplasty (PTCA), arteriosclerosis, thrombosis (e.g., acute-phase cerebral thrombosis, pulmonary embolism), hypertension, pulmonary hypertension, ischemic disorder (e.g., cerebral infarction, myocardial infarction), angina (e.g., stable angina, unstable angina), glomerulonephritis, diabetic nephropathy, chronic renal failure, allergy, bronchial asthma, ulcer, pressure ulcer (bedsore), restenosis after coronary intervention such as atherectomy and stent implantation, thrombocytopenia by dialysis, the diseases in which fibrosis of organs or tissues is involved [e.g., Renal diseases (e.g., tuburointerstitial nephritis), respiratory diseases (e.g., interstitial pneumonia (pulmonary fibrosis), chronic obstructive pulmonary disease), digestive diseases (e.g., hepatocirrhosis, viral hepatitis, chronic pancreatitis and scirrhous stomachic cancer), cardiovascular diseases (e.g, myocardial fibrosis), bone and articular diseases (e.g, bone marrow fibrosis and rheumatoid arthritis), skin diseases (e.g, cicatrix after operation, scalded cicatrix, keloid, and hypertrophic cicatrix), obstetric diseases (e.g., hysteromyoma), urinary diseases (e.g., prostatic hypertrophy), other diseases (e.g., Alzheimer's disease, sclerosing peritonitis; type I diabetes and organ adhesion after operation)], erectile dysfunction (e.g., diabetic erectile dysfunction, psychogenic erectile dysfunction, psychotic erectile dysfunction, erectile dysfunction associated with chronic renal failure, erectile dysfunction after intrapelvic operation for removing prostata, and vascular erectile dysfunction associated with aging and arteriosclerosis), inflammatory bowel disease (e.g., ulcerative colitis, Crohn's disease, intestinal tuberculosis, ischemic colitis and intestinal ulcer associated with Behcet disease), gastritis, gastric ulcer, ischemic ophthalmopathy (e.g., retinal artery occlusion, retinal vein occlusion, ischemic optic neuropathy), sudden hearing loss, avascular necrosis of bone, intestinal damage caused by administration of a non-steroidal anti-inflammatory agent (e.g., diclofenac, meloxicam, oxaprozin, nabumetone, indomethacin, ibuprofen, ketoprofen, naproxen, celecoxib) (there is no particular limitation for the intestinal damage so far as it is damage appearing in duodenum, small intestine and large intestine and examples thereof include mucosal damage such as erosion and ulcer generated in duodenum, small intestine and large intestine), and symptoms associated with lumbar spinal canal stenosis (e.g., paralysis, dullness in sensory perception, pain, numbness, lowering in walking ability, etc. associated with cervical spinal canal stenosis, thoracic spinal canal stenosis, lumbar spinal canal stenosis, diffuse spinal canal stenosis or sacral stenosis) etc. (see, for example, in WO '084, WO 2009/157396, WO 2009/107736, WO 2009/154246, WO 2009/157397, and WO 2009/157398).

In addition, compound A is useful as an accelerating agent for gene therapy or angiogenesis therapy such as autologous bone marrow transplantation, an accelerating agent for angiogenesis in restoration of peripheral artery or angiogenic therapy, etc. (see, for example, in WO '084).

As mentioned above, while the usefulness of compound A as therapeutic agents for the above-mentioned disorders is known, no reference describes or suggests the possibility of existence of crystals of compound A.

BRIEF SUMMARY OF THE INVENTION

A main object of the present invention is to provide a novel crystal of compound A. Additionally, an object of the present invention is to provide a method for producing the crystal, and a pharmaceutical composition containing the crystal as an active ingredient.

It is hoped that medicament bulk is a thing of a high quality for which constant effect can be always shown and of a form which is handled easily industrially. The present inventors have earnestly studied. As a result, the present inventors have found a novel crystal of compound A, and have completed the present invention.

The present invention includes, for example, the following aspects.

One aspect is Form-I crystal of compound A which shows diffraction peaks in the powder X-ray diffraction spectrum of compound A (hereinafter referred to as "Form-I crystal of the invention") at the following angles of diffraction 2θ: 9.4